## REMARKS

Claims 1-2 and 4-13 are pending in the application. Claim 1 has been amended to clarify what it is that the applicants regard as their invention. Moreover, claim 13 has been added to the application. Claim 13 describes one preferred embodiment of the invention that is believed to be patentable, along with claims 1-2 and 4-12 over the prior art of record. No new matter has been added to the application by way of these claim amendments.

The Examiner's claim rejection is overcome as set forth below.

### I. The Obviousness Rejection Of Claims 1-2 and 4-12

Claims 1-2 and 4-12 were rejected under 35 U.S.C. 103(a) as being unpatentable over McCormick et al., in view of Copeland et al. and further in view of the McManus et al. article. It is the Examiner's position that McCormick et al. teaches most aspects of the claimed invention except for the mixing of reagents on a slide and using unstable staining solutions. The Examiner looks to the Copeland et al. reference for teaching the steps of applying a reagent staining solution to a slide and mixing the solution on the surface of the slide by applying a gas stream or two gas streams so as to form a vortex. The Examiner further takes the position that McManus et al. discloses unstable staining solutions and that it would have been obvious to combine McManus et al. with Copeland et al. because Copeland et al. discusses applying multiple "reagents" to a biological sample.

The Examiner's obviousness rejection is overcome as set forth below.

#### A. The Obviousness Rejection Is Based Upon An Improper Hindsight Analysis Of The Prior Art – There Is No Suggestion (Except In Applicants Invention) To Combine McManus et al. with Copeland et al. or with McCormick et al. As The Examiner Has

The Examiner's obviousness rejection is based upon an improper hindsight analysis of the prior art with the applicants' invention in mind. For this reason, the Examiner should withdraw the obviousness rejection of all claims.

In finally rejecting all claims for obviousness, the Examiner has clearly first considered the

Applicants' invention and then has viewed the prior art references in hindsight – with the Applicant's invention in mind. This is not the correct obviousness analysis. "Measuring a claimed invention against the standard established by section 103 requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field." *See, e.g.* , *W.L. Gore & Assoc., Inc. v. Garlock, Inc.* , 721 F.2d 1540, 1553, 220 UPSQ 303, 313 (Fed. Cir. 1983). Adherence to this methodology is important where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." *Id.*

There is absolutely no teaching or suggestion in the prior art cited the Examiner that the several ingredients of an unstable staining solution my be applied independently and before mixing to a biological sample and thereafter allowed to form an unstable staining solution in contact with the biological material. Moreover, there is no teaching or suggestion that the individual ingredients are "reagents" as that term is understood by a person of ordinary skill in the art. What the Examiner has done is to evaluate the prior art in hindsight – he was aware that the claims called for applying the components of an unstable staining solution to a biological sample and then he found the invention in the prior art.

When considered for their teachings alone, one of ordinary skill in the art would not have combined the references as the Examiner has to obtain the claimed invention. The McManus et al. reference discloses several unstable staining solutions. The staining solutions are premixed to form useful "reagents" and then applied as a single unstable staining solution to a biological sample. There is absolutely no disclosure or suggestion in McManus et al. that the individual ingredients used to formulate the unstable staining solution (1) can be applied independently to a biological sample to form an unstable staining solution in contact with the biological sample; or (2) are useful individually as "reagents" as that term is used in the art.

The Copeland and McCormick et al. references disclose automated laboratory analysis systems. The references disclose applying various "reagents", rinsing solutions, buffers and so forth to biological samples during automated histochemical and staining processes. There is absolutely no suggestion in either McCormick et al. or Copeland et al. that ingredients used to

formulate an unstable staining solution can be independently applied to a biological sample.

The Applicant's position is simple. Without the present application before him, the Examiner would not have understood the prior art to disclose or suggest sequentially applying the stable ingredients of unstable staining solutions to a biological sample to form an unstable solution in contact with a biological sample. Instead, the Examiner would have understood the prior art to disclose applying a pre-mixed and unstable staining solutions as a reagents to a biological sample. The Examiner's obviousness rejection should, therefore be withdrawn because it is based on improper hindsight analysis of the prior art.

### B. The Prior Art Does Not Disclose Or Suggest Applying Two Reagents Sequentially To A Biological Sample To Form An Unstable Solution

Each of the application claims, including new claim 13, is directed to the "sequential" application of first and second stable solutions to a biological material to form an unstable staining solution. This aspect of the invention is described in the specification and Examples. In Example 1, for example, the steps of an automated histochemical assay are identified. Steps 21-23 relate to the application of two stabile solutions to form an unstable solution. Steps 21-23 occur sequentially with only the application of a liquid coverslip occurring between the two stable solution application steps. Such a sequential application of stable reagents to form an unstable staining solution is not disclosed or suggested in the prior art. Moreover new claim 13 expressly requires sequential application of solutions without rinsing the sample in between solution applications. For this reason alone, claims 1-2 and 4-13 are non-obvious of the prior art of record.

In the April 21, 2003 Final Rejection, the Examiner stated that "the Copeland reference did teach the sequential application of several solutions that cumulatively allow histologic study of the sample .... Copeland generally refers to the solutions brought into contact with the samples as reagents. This implies that any reagent known in the art may be applied using a method and apparatus disclosed in the reference." The Examiner goes on to recite column 20, lines 24-42 of Copeland in support of this interpretation of their reference.

Copeland does not, as the Examiner maintains, disclose the "sequential" application of solutions onto a biological sample as that term is used in the claims. The passage of the Copeland

et al. recited by the Examiner is merely one of several steps of "a typical immunohistological method." When read in its entirety, the steps in the method disclosed in Copeland et al. do not teach sequential addition of reagents. Instead, Copeland discloses steps of (1) applying a single reagent to a biological sample, and (2) thereafter subjecting the sample to several additional processing steps and only then possibly applying a second reagent to this slide. This understanding of Copeland et al. finds support, for example, at column 9, lines 19-29 which teaches:

> As the slide support carousel 24 positions each slide for successive treatment in the rinse zones, evaporation inhibitor and reagent application zone, and agitation zones (counterclockwise movement of the carousel), the tissue sections on each slide are first rinsed and then covered with evaporation inhibitor. Reagent is applied from a preselected reagent bottle to the tissue through the evaporation inhibitor layer, and the reagent is agitated through the evaporator inhibitor layer by the vortex mixer. Each slide then is moved around the incubation zone, a circular path traveled by the slide support carousel 24, heated with hot air from the heated air manifold 30, and the reagent reacts with the sample. <u>As the carousel 24 continues to increment around the circle, each slide is returned to the rinse stations, etc, for application of the next reagent required in the reaction</u>. This entirely automated process continues Until the desired reactions are completed.

(Emphasis added) This excerpt from Copeland et al., which is consistent with the teachings of Copeland et al. as a whole, including the portion of the reference cited by the Examiner, makes it clear that only one reagent is applied to a biological sample the during each trip through the reagent application zone. Moreover, steps such as air agitation, rinsing etc. . . are performed on the reagent containing sample before a second reagent is applied to the sample. No where does Copeland disclose or suggest that more than one reagent can be "sequentially" applied to the biological sample, i.e., applied to the biological sample without performing significant intervening processing steps between reagent applications.

One of ordinary skill in the art would understand that Copeland et al., as a whole, does not disclose a process whereby reagents are "sequentially" applied (without intervening process steps) to a biological sample as claimed. Moreover, the McMannus et al. and the McCormick et al. reference do not disclose sequential application of stable reagents to a biological sample to form an unstable solution. For this reason, the Examiner has not established a *prima facie* case of obviousness because the combination of references cited by the Examiner does not disclose every

element of the claimed invention.

**C. The Applicant's 1/25/03 Traversal Was Adequate**

The Examiner suggests in the April 21, 2003 Final Rejection that the applicants 1/25/03 traversal of the obviousness rejection premised upon McCormick et al., Copeland et al. and McManus et al. was insufficient because only two of the three references were discussed in the traversal. The Applicant's traversal was sufficient. Where, as here, it is the Applicants' position that one of several prior art references lack a teaching relied upon by the Examiner to establish a *prima facie* case of obviousness, there is no need for the Applicants to discuss other references that were not cited by the Examiner for supplying the missing teaching. It is Applicants' position that the rejections based upon the Copeland et al and McCormick et al. references did not establish a *prima facie* case of obviousness. That position did not change when McManus et al. was included as a reference. Finally, the McManus et al. reference was clearly identified in the heading of the traversal so its inclusion in the traversal discussion is implied.

**Conclusion**

For the reasons indicated above, claims 1–2 and 4-13 are believed to be patentable over the prior art of record. Favorable reconsideration and allowance of the pending application is, therefore, courteously solicited.

Respectfully submitted,

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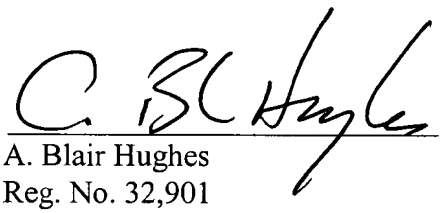
By: 

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